

01/09

EXENDIN-3

His	Ser	Asp	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Met	Glu	Glu
1				5					10					15	
Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser
		20						25					30		
Ser	Gly	Ala	Pro	Pro	Pro	Ser-NH ₂									
		35													

Fig. 1

EXENDIN-4

His	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Met	Glu	Glu
				5					10					15	
Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser
			20					25					30		
Ser	Gly	Ala	Pro	Pro	Pro	Ser-NH ₂									
		35													

*Fig. 2*GLP-1 (GLP-1 [7-36]NH₂)

His	Ala	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Val	Ser	Ser	Tyr	Leu	Glu	Gly
				5					10					15	
Gln	Ala	Ala	Lys	Glu	Phe	Ile	Ala	Trp	Leu	Val	Lys	Gly	Arg-NH ₂		
			20					25					30		

Fig. 3

09/5/4333

Antico Acid Position	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38		
Compound 1	His	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Met	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly		Gly	NH2									
Compound 2	His	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Met	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	NH2												
Compound 3	His	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Met	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Phe	Leu	Lys	Asn	NH2												
Compound 4	His	Ala	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Met	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Phe	Leu	Lys	Asn	NH2												
Compound 5	His	Gly	Glu	Gly	Ala	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Leu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Phe	Leu	Lys	Asn	NH2												
Compound 6	His	Gly	Glu	Gly	Thr	Ala	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Leu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Phe	Leu	Lys	Asn	NH2												
Compound 7	His	Gly	Glu	Gly	Thr	Phe	Thr	Ala	Asp	Leu	Ser	Lys	Gln	Leu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Phe	Leu	Lys	Asn	NH2												
Compound 8	His	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Ala	Ser	Lys	Gln	Leu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Phe	Leu	Lys	Asn	NH2												
Compound 9	His	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ala	Lys	Gln	Leu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Phe	Leu	Lys	Asn	NH2												
Compound 10	His	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Ala	Gln	Leu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Phe	Leu	Lys	Asn	NH2												
Compound 11	His	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Ala	Leu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Phe	Leu	Lys	Asn	NH2												
Compound 12	His	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Ala	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Phe	Leu	Lys	Asn	NH2												
Compound 13	His	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Leu	Ala	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Phe	Leu	Lys	Asn	NH2												
Compound 14	His	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Leu	Glu	Ala	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Phe	Leu	Lys	Asn	NH2											
Compound 15	His	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Leu	Glu	Ala	Ala	Val	Arg	Leu	Phe	Ile	Glu	Phe	Leu	Lys	Asn	NH2												
Compound 16	His	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Leu	Glu	Glu	Ala	Ala	Arg	Leu	Phe	Ile	Glu	Phe	Leu	Lys	Asn	NH2												
Compound 17	His	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Leu	Glu	Ala	Val	Ala	Leu	Phe	Ile	Glu	Phe	Leu	Lys	Asn	NH2													
Compound 18	His	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Leu	Glu	Glu	Ala	Val	Arg	Ala	Phe	Ile	Glu	Phe	Leu	Lys	Asn	NH2												
Compound 19	His	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Leu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Phe	Leu	Lys	Asn	NH2												
Compound 20	His	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Leu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Ala	Leu	Lys	Asn	NH2												
Compound 21	His	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Leu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Phe	Ala	Lys	Asn	NH2												
Compound 22	His	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Leu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Phe	Leu	Ala	Lys	Asn	NH2											
Compound 23	His	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Leu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Phe	Leu	Lys	Asn	NH2												
Compound 24	His	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Met	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Gly	Ala	Pro	Pro	Pro	NH2			
Compound 25	His	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Met	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Gly	Ala	Pro	Pro	Pro	NH2			
Compound 26	His	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Met	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Gly	Ala	Pro	Pro	Pro	NH2			
Compound 27	His	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Leu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Gly	Ala	Pro	Pro	Pro	NH2			
Compound 28	His	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Met	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Gly	Ala	Pro	Pro	Pro	NH2			
Compound 29	His	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Leu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Gly	Ala	Pro	Pro	Pro	NH2			
Compound 30	His	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Met	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Gly	Ala	Pro	Pro	Pro	NH2			
Compound 31	His	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Leu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Gly	Ala	Pro	Pro	Pro	NH2			
Compound 32	His	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Met	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Gly	Ala	Pro	Pro	Pro	NH2			
Compound 33	His	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Leu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Gly	Ala	Pro	Pro	Pro	NH2			
Compound 34	His	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Met	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Gly	Ala	Pro	Pro	Pro	NH2			
Compound 35	His	Gly	Glu	Gly	Thr	Phe	Thr	Ser	Asp	Leu	Ser	Lys	Gln	Leu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Gly	Ala	Pro	Pro	Pro	NH2			

Fig. 4A

03/09

Amino Acid Position	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38
Compound 36	His	Gly	Gly	Gly	Thr	Thr	Thr	Thr	Asp	Leu	Ser	Lys	Gln	Met	Glu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	NH2					
Compound 37	His	Gly	Gly	Gly	Thr	Thr	Thr	Thr	Asp	Leu	Ser	Lys	Gln	Glu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Phe	Leu	Lys	Asn	Gly	Gly	Pro	Ser	NH2						
Compound 38	His	Gly	Gly	Gly	Thr	Thr	Thr	Thr	Asp	Leu	Ser	Lys	Gln	Met	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	NH2							
Compound 39	His	Gly	Gly	Gly	Thr	Thr	Thr	Thr	Asp	Leu	Ser	Lys	Gln	Glu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Phe	Leu	Lys	Asn	Gly	Gly	Pro	NH2							
Compound 40	His	Gly	Gly	Gly	Thr	Thr	Thr	Thr	Asp	Leu	Ser	Lys	Gln	Glu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Phe	Leu	Lys	Asn	Gly	Gly	NH2								
Compound 41	His	Gly	Gly	Gly	Thr	Thr	Thr	Thr	Asp	Leu	Ser	Lys	Gln	Met	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	NH2									
Compound 42	His	Gly	Gly	Gly	Thr	Thr	Thr	Thr	Asp	Leu	Ser	Lys	Gln	Glu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Phe	Leu	Lys	Asn	Gly	NH2									
Compound 43	His	Gly	Gly	Gly	Thr	Thr	Thr	Thr	Asp	Leu	Ser	Lys	Gln	Met	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Ser	Gly	Ala	Pro	Pro	NH2	
Compound 44	His	Gly	Gly	Gly	Thr	Thr	Thr	Thr	Asp	Leu	Ser	Lys	Gln	Met	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Nme	Ser	Ser	Gly	Ala	Nme	Nme	NH2	
Compound 45	His	Gly	Gly	Gly	Thr	Thr	Thr	Thr	Asp	Leu	Ser	Lys	Gln	Met	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	hPro	Ser	Ser	Gly	Ala	hPro	hPro	NH2	
Compound 46	His	Gly	Gly	Gly	Thr	Thr	Thr	Thr	Asp	Leu	Ser	Lys	Gln	Met	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	hPro	Ser	Ser	Gly	Ala	hPro	hPro	NH2	
Compound 47	His	Gly	Gly	Gly	Thr	Thr	Thr	Thr	Asp	Leu	Ser	Lys	Gln	Met	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	hPro	Ser	Ser	Gly	Ala	hPro	hPro	NH2	
Compound 48	His	Gly	Gly	Gly	Thr	Thr	Thr	Thr	Asp	Leu	Ser	Lys	Gln	Met	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Ser	Gly	Ala	NH2			
Compound 49	Arg	Gly	Gly	Gly	Thr	Thr	Thr	Thr	Asp	Leu	Ser	Lys	Gln	Met	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	NH2								
Compound 50	His	Gly	Asp	Gly	Thr	Thr	Thr	Thr	Asp	Leu	Ser	Lys	Gln	Met	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Phe	Leu	Lys	Asn	NH2										
Compound 51	His	Gly	Gly	Gly	Thr	Thr	Thr	Thr	Asp	Leu	Ser	Lys	Gln	Met	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	NH2										
Compound 52	His	Gly	Gly	Gly	Thr	Thr	Thr	Thr	Asp	Leu	Ser	Lys	Gln	Met	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	NH2										
Compound 53	His	Gly	Gly	Gly	Thr	Thr	Thr	Thr	Asp	Leu	Ser	Lys	Gln	Met	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	NH2										
Compound 54	His	Gly	Gly	Gly	Thr	Thr	Thr	Thr	Asp	Gly	Ser	Lys	Gln	Met	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Phe	Leu	Lys	Asn	NH2										
Compound 55	His	Gly	Gly	Gly	Thr	Thr	Thr	Thr	Asp	Leu	Ser	Lys	Gln	Glu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Phe	Leu	Lys	Asn	NH2										
Compound 56	His	Gly	Gly	Gly	Thr	Thr	Thr	Thr	Asp	Leu	Ser	Lys	Gln	Glu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	NH2										
Compound 57	His	Gly	Gly	Gly	Thr	Thr	Thr	Thr	Asp	Leu	Ser	Lys	Gln	Met	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Phe	Leu	Lys	Asn	NH2										
Compound 58	His	Gly	Gly	Gly	Thr	Thr	Thr	Thr	Asp	Leu	Ser	Lys	Gln	Glu	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Phe	Leu	Lys	Asn	Gly	Gly	Pro	Ser	Ser	NH2					
Compound 59	His	Gly	Gly	Gly	Thr	Thr	Thr	Thr	Asp	Ala	Ser	Lys	Gln	Met	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Phe	Leu	Lys	Asn	Gly	Gly	NH2								
Compound 60	His	Gly	Gly	Gly	Thr	Thr	Thr	Thr	Asp	Ala	Ser	Lys	Gln	Met	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	NH2									
Compound 61	His	Gly	Gly	Gly	Thr	Thr	Thr	Thr	Asp	Ala	Ser	Lys	Gln	Met	Glu	Glu	Ala	Val	Arg	Leu	Phe	Ile	Glu	Trp	Leu	Lys	Asn	Gly	Gly	hPro	Ser	Ser	Gly	Ala	hPro	hPro	NH2	

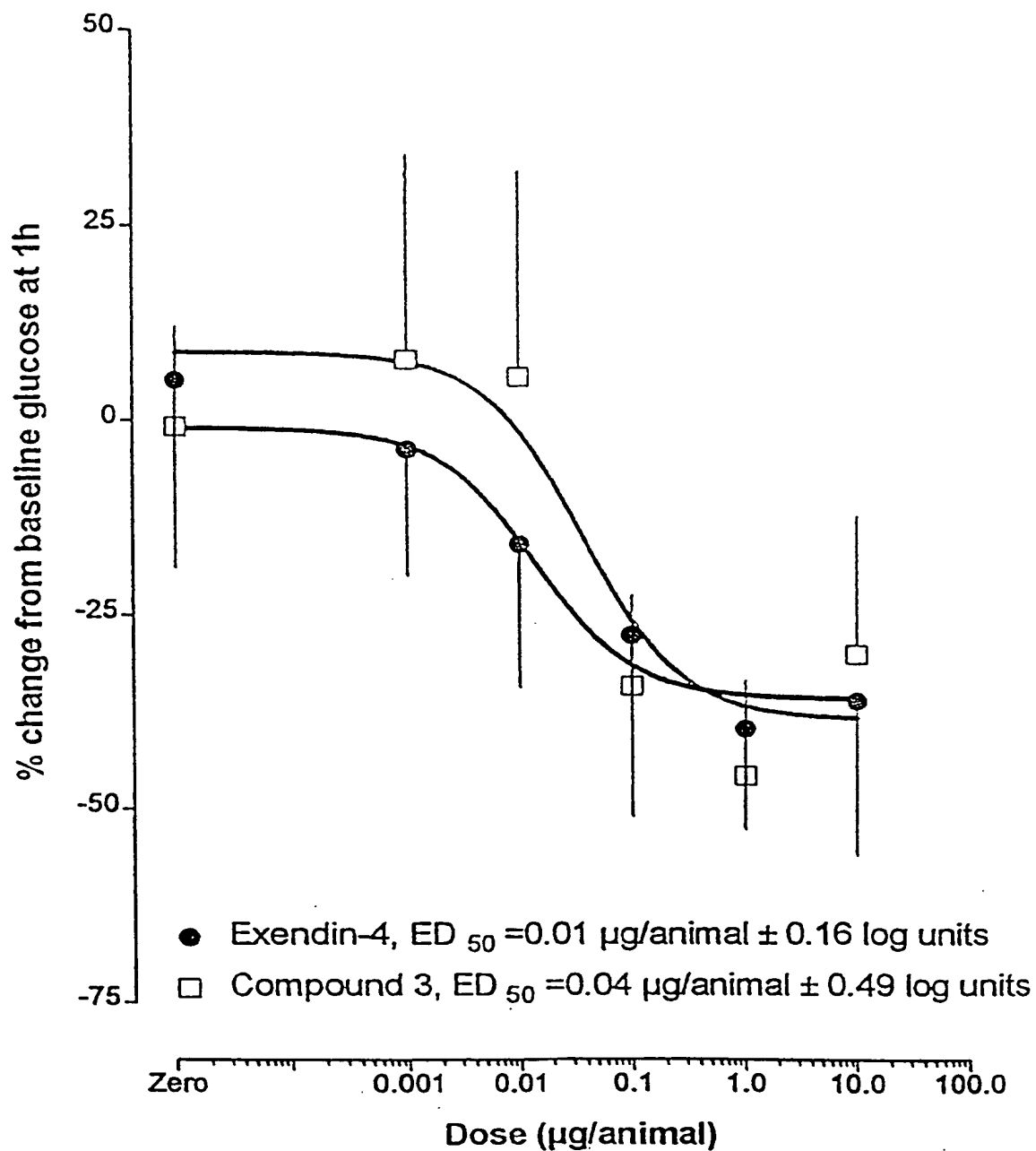
Fig. 4B

SUBSTITUTE SHEET (RULE 26)

BEST AVAILABLE COPY

04/09

Glucose lowering effect in db/db mice at 1 hr time point

**Fig. 5**

SUBSTITUTE SHEET (RULE 26)

05/09

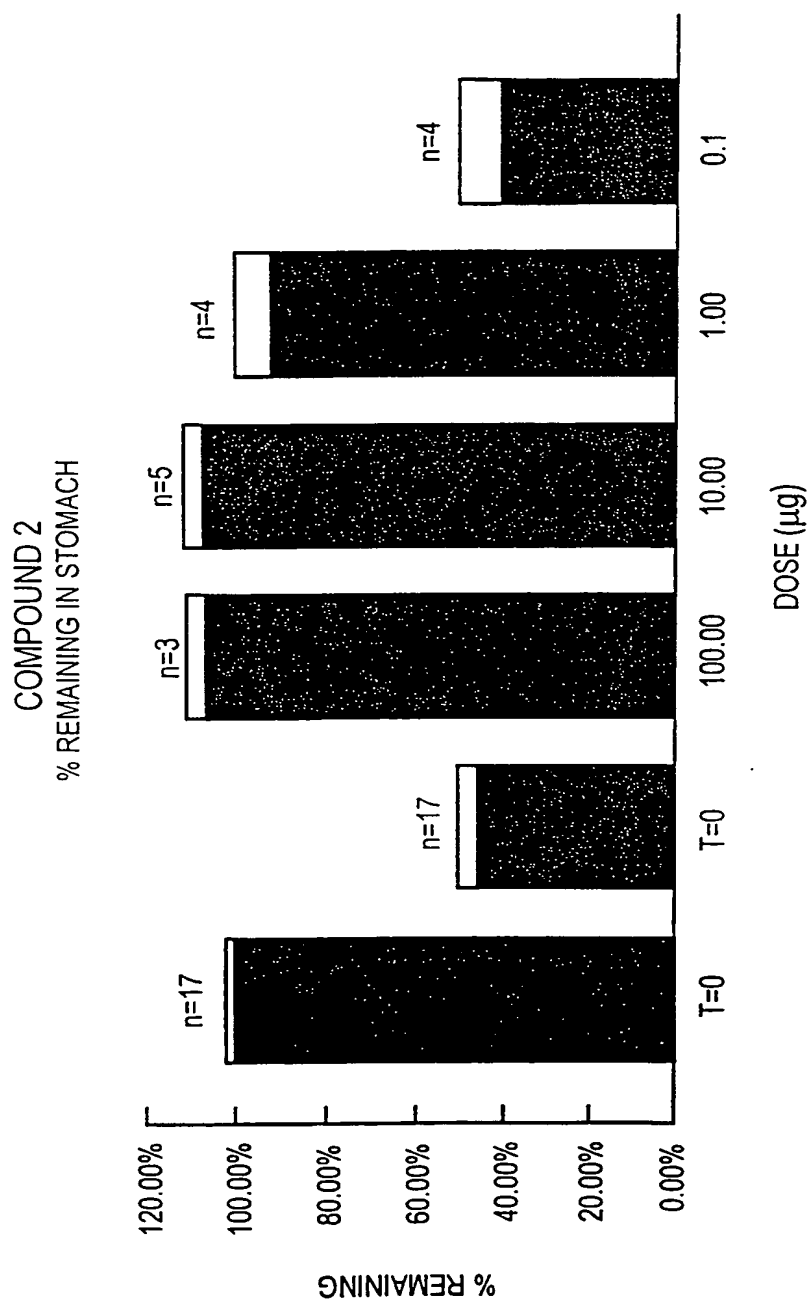


Fig. 6

06/09

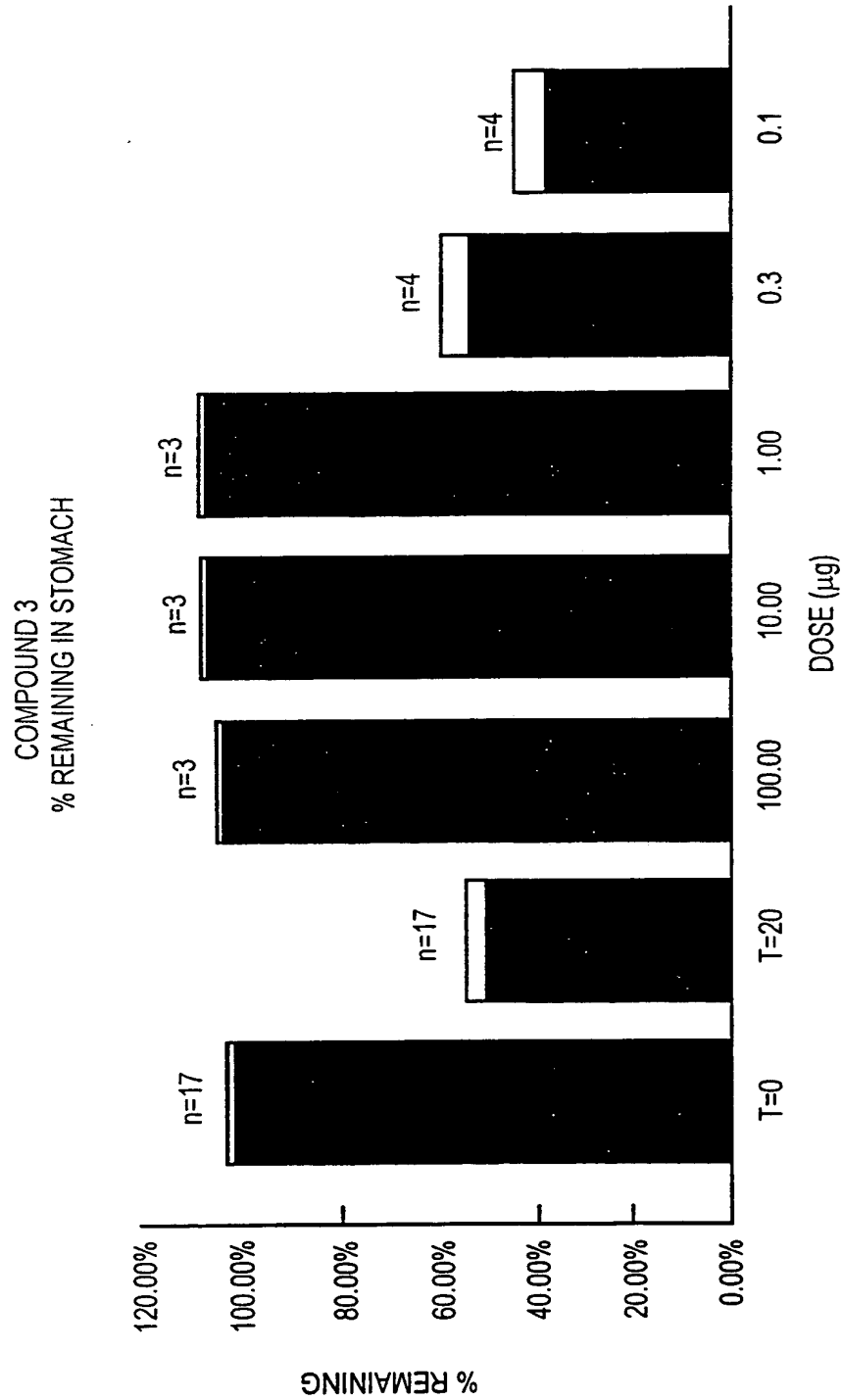


Fig. 7

07/09

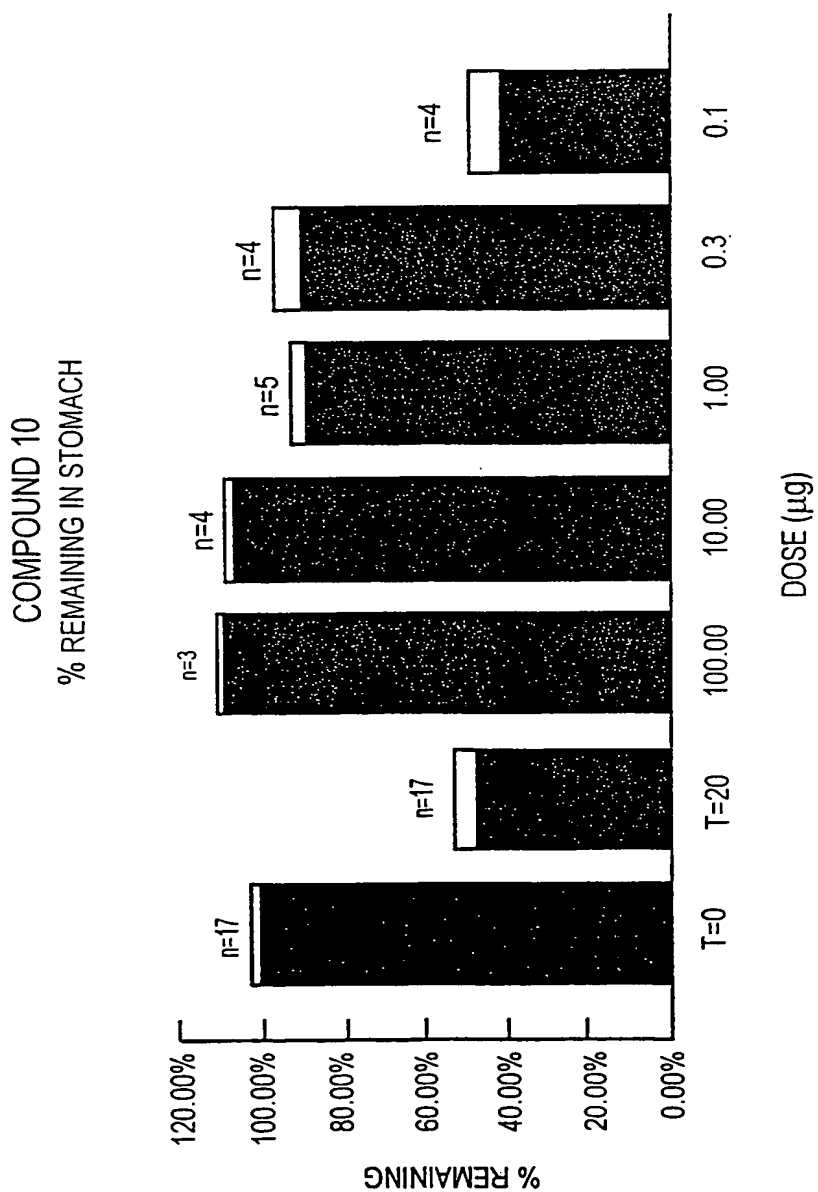


Fig. 8

08/09

COMPOUND 13
% REMAINING IN STOMACH

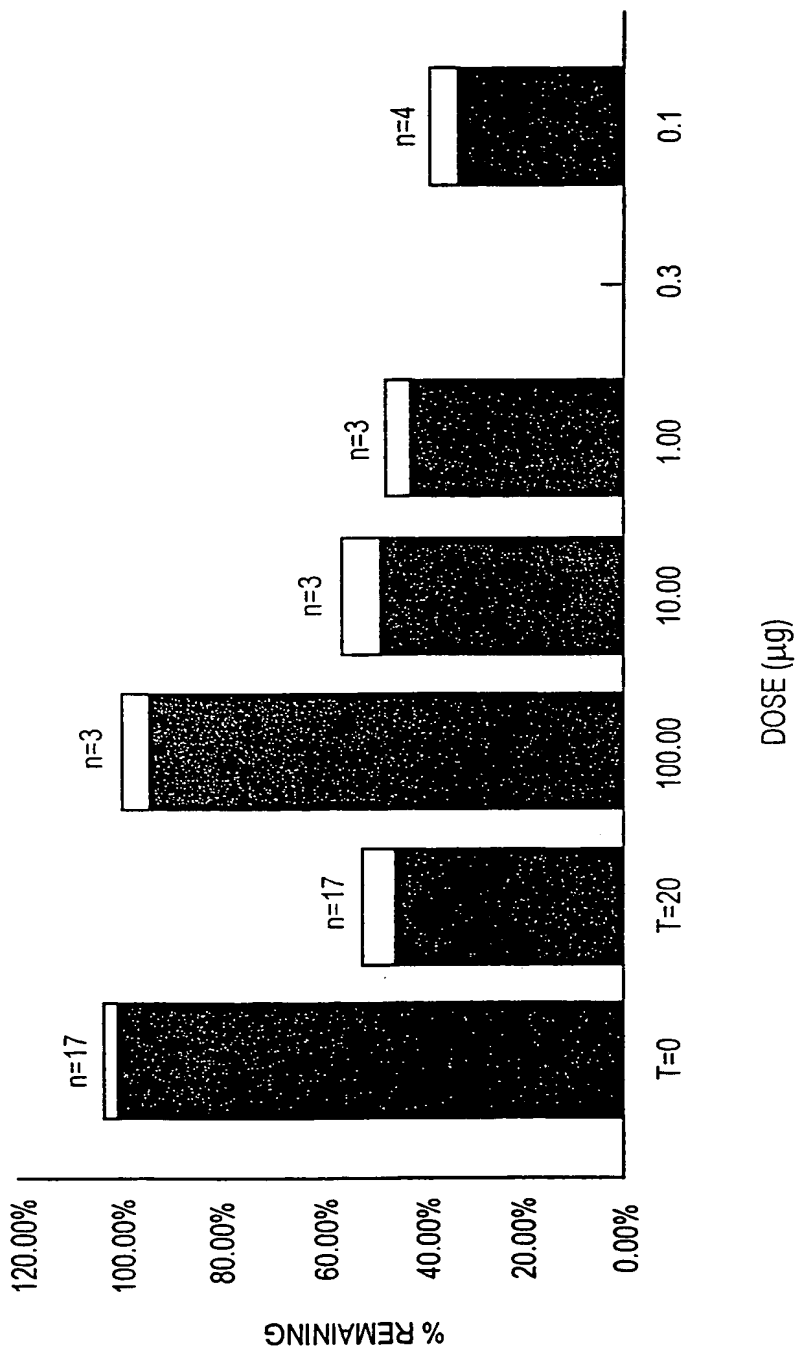


Fig. 9

09/09

Compound
No.

- 62 4-Imidazolylpropionyl-Gly Glu Gly Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Ala Val Arg Leu
Phe Ile Glu Trp Leu Lys-NH⁺octanoyl Asn-NH₂, [SEQ. ID NO. 67]
- 63 4-Imidazolylpropionyl-Gly Glu Gly Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Ala Val Arg Leu
Phe Ile Glu Phe Leu Lys-NH⁺octanoyl Asn-NH₂, [SEQ. ID NO. 68]
- 64 4-Imidazolylpropionyl-Gly Glu Gly Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Ala Val Arg Leu
Phe Ile Glu Trp Leu Lys-NH⁺octanoyl Asn Gly Gly-NH₂, [SEQ. ID NO. 69]
- 65 4-Imidazolylpropionyl-Gly Glu Gly Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Ala Val
Arg Leu Phe Ile Glu Phe Leu Lys-NH⁺octanoyl Asn Gly Gly-NH₂, [SEQ. ID NO. 70]
- 66 4-Imidazolylpropionyl-Gly Glu Gly Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Ala Val Arg Leu
Phe Ile Glu Trp Leu Asn Lys-NH⁺octanoyl-NH₂, [SEQ. ID NO. 71]
- 67 4-Imidazolylpropionyl-Gly Glu Gly Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Ala Val Arg Leu
Phe Ile Glu Phe Leu Asn Lys-NH⁺octanoyl-NH₂, [SEQ. ID NO. 72]
- 68 4-Imidazolylpropionyl-Gly Glu Gly Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Ala Val Arg Leu
Phe Ile Glu Trp Leu Asn Lys-NH⁺octanoyl Gly Gly-NH₂, [SEQ. ID NO. 73]
- 69 4-Imidazolylpropionyl-Gly Glu Gly Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Ala Val Arg Leu
Phe Ile Glu Phe Leu Asn Lys-NH⁺octanoyl Gly Gly-NH₂, [SEQ. ID NO. 74]

Fig. 10